

SECOND DECLARATION FOR BCS 03-3056 US

DECLARATION UNDER 37 CFR 1.132

I, Andreas Guenther, of Kuckelbergweg 3a, 51069 Cologne, Germany, declare as follows:

1. I studied at the University of Hannover, Germany, where I obtained a degree of doctor rer. nat. in chemistry. Since September 1, 1980, I have been employed by Bayer AG, Leverkusen, Germany, and remain employed in the process department IOP-IND with Bayer CropScience AG in Dormagen, Germany. I specialize in the field of process chemistry.

2. I am an inventor of, and I am familiar with the subject matter disclosed in the present United States patent application no. 10/668,356 ("the '355 application").

3. I have reviewed WO 02/16304 to Müh *et al.* ("the Müh reference") which has been cited against the claims of the '355 application.

4. Attached herewith as Exhibits A, B and C are true and accurate English language translations of business records prepared and maintained in the ordinary course of business of a laboratory of Bayer AG, Leverkusen, Germany. A copy of each record in the German language as originally prepared is appended to its respective English language translation. I have reviewed the records of Exhibits A, B and C in making this Declaration.

5. Exhibit A is a record dated May 23, 2000, of a protocol of an experiment carried out under the supervision of Dr. Müh that corresponds to Example 1 described in the Müh reference. As provided in the experiment of Exhibit A, the reaction yielded approximately 85% of fluoromalonic ester product using 3 equivalents of reactants (triethylamine and hydrogen fluoride) per equivalent diethyl chloromalonate. In particular, 494 g of triethylamine bishydrofluoride and 357 g triethylamine were heated to 105°C, and 535 g of diethyl chloromalonate was metered in over 8 hours. The reaction mixture was stirred at 105°C, and the reaction time was 12 hours at an inherent pressure of just under 6 bar.

6. Accordingly, the experiment of Exhibit A shows that, under the method described in Example 1 of the Müh reference, for the documented reaction

temperature of about 105°C and the reaction time of 12 hours, the reaction pressure was just under 6 bar.

7. Exhibit B is a record dated July 21, 2000, of a general description of the method used in the Examples 1 and 2 of the Müh reference, this general description differing from the Examples of the Müh reference in the amounts of the reagents used. The general description indicates that the pressure-resistant reaction vessel was sealed so as to be pressure-sealed after adding the reagents of triethylamine and hydrogen fluoride into the vessel, and then the contents of triethylamine and hydrogen fluoride were heated to 105°C. Diethyl chloromalonate was metered in within 6 hours and the mixture was stirred for an additional 6 hours at 105°C. Accordingly, the reaction time in the pressure-resistant reaction vessel at 105°C was 12 hours. The general description of the method provided by the Exhibit B record was used to carry out the experiment of Exhibit A and the experiment of Exhibit C, described below.

8. Exhibit C is a record dated October 30, 2000, of an internal order for an experiment carried out on behalf of Dr. Pleschke. This experiment corresponds to Example 2 described in the Müh reference in which 2 equivalents of reactants (triethylamine and hydrogen fluoride) per equivalent diethyl chloromalonate are used. The internal order includes a two page attachment of time, temperature and pressure data monitored during the experiment.

9. As provided in the experiment of Exhibit C, the reaction was conducted in a 3 liter autoclave, in which the reactants were heated to 105°C. When the metering of the chloromalonic ester was started (at time 14:30), the documented operating temperature and pressure were 102°C and 3.5 bar. When the metering was stopped about 6 hours later (at time 20:25), the operating temperature and pressure were 105°C and 5.6 bar. After an additional reaction time of 6 hours (at time 2:25), the documented operating temperature and pressure were 104.7°C and 6.9 bar.

10. Accordingly, the experiment of Exhibit C shows that, under the method described in Example 2 of the Müh reference, for the documented reaction temperature of about 105°C and the reaction time of 12 hours, the reaction pressure ranged from 3.5 bar to 6.9 bar.

11. In comparison to the experiments of Exhibits A and C, Example 1 of the '355 application shows that for the reaction temperature of 105 to 110°C under normal pressure (800 to 1200 mbar), the reaction time is 15 hours.

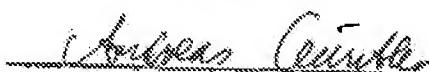
12. Thus, the method of the Müh reference requires a reaction pressure about 5 times higher than that of the '355 application in order to achieve a comparable short reaction time of 12 hours.

13. In my opinion, one of skill in the art, attempting to achieve a short reaction time for preparing dialkyl alpha-fluoromalonates, would not have been led by the teachings of the Müh reference to reduce the pressure to normal pressure since the method of Müh reference clearly requires the reaction to be conducted under increased pressure, and further requires such increased pressure to be significantly higher than normal pressure, at almost 8 bar and higher, to achieve the short reaction time of 12 hours.

14. In addition, U.S. Patent No. 5,391,811 to Bohm *et al.* ("Bohm"), discussed in the Declaration under 37 CFR 1.132 executed by me on December 22, 2008, describes a method carried out under normal pressure in which the reaction time is 72 hours. In light of the long reaction time described in the Bohm reference, in my opinion, one of skill in the art would not have been led to reduce the pressure of the method of the Müh reference to normal pressure to achieve a short reaction time.

6. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Signed at Dormagen, this 2nd day of June, 2010.



Andreas Guenther

Draft Rule 132 Declaration of Dr. Guenther.DOC 3 of 3

Exhibit A

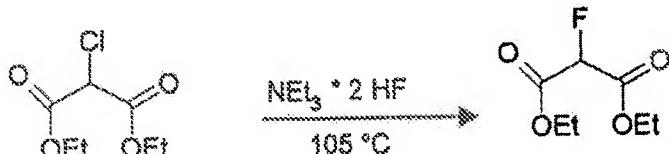
Project: HEC 572S **Date of test:** 23.05.00

Stage/procedure variant: Fluoromalonic ester **Carried out by:** Muscara

Test No.: MUEH 9/34 Head of laboratory: Dr Mühl

Notes:

Reaction equation:



Diethyl chloromalonate
194.5 g/mol

Diethyl fluoromalonate
178 g/mol

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Weight (g)	(mol)	Purity (%)	
535	2.33	84.7	Diethyl chloromalonate MUEH 14/25 (3.2% diethyl malonate, 15.2% diethyl dichloromalonate)
494	3.5	100	Triethylamine bishydrofluoride (Fluorlabor)(0.18% water)
357	3.5	99	Triethylamine (Riedel de Haen)

Description of the test

Introduce triethylamine bishydrofluoride and triethylamine, heat to 105°C, then meter in diethyl chloromalonate over 6 h.

Continue stirring the mixture at 105°C until measurements show that the development of heat has ceased.

The reaction time under an inherent pressure of just under 6 bar was 12 hours.

After the reaction has ended, the mixture is cooled to RT, and 494.5 g of water are added to dissolve the suspension. Record the amount of reaction mixture removed for further DTA tests.

1618 g of final reaction mixture were worked up with 12 g of crystal complexes (which are soluble in 50 g of water).

After phase separation, 525 g of organic and 1093 g of aqueous phase are obtained; the latter does not contain any product.

Yield: approximately 85% of product

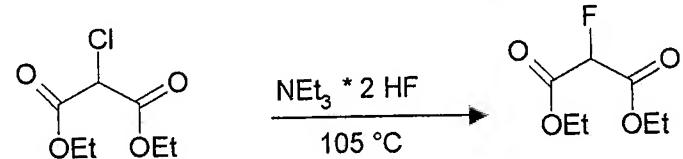
$m = 525 \text{ g}$ $GC_{ISTD} = 67.2\%$

Test A as described in WO 02/16304 (Müh)

Projekt:	HEC 5725	Versuchsdatum:	23.05.00
Stufe/Verfahrensvariante:	Fluormalonester	Durchführende :	Muscaria
Versuchs-Nr.: MUEH 9/34		Laborleiter:	Dr. Müh

Bemerkung :

Reaktionsgleichung:

Chlormalonsäure-
diethylester
194,5 g / molFluormalonsäure-
diethylester
178 g / mol

Einsatzstoffe

Massen (g)	(mol)	Gehalt (%)	
535	2,33	84,7	Chlormalonsäurediethylester MUEH 14/25 (3,2 %Malonsäurediethylester, 15,2 % Dichlormalonsäurediethylester)
494	3,5	100	Triethylamin-Bishydrofluorid (Fluorlabor)(0,18 % Wasser)
357	3,5	99	Triethylamin (Riedel de Haen)

VERSUCHSDIREKTIION

Das Triethylamin-Bishydrofluorid und Triethylamin vorlegen und auf 105°C aufheizen, anschließend in 6 h den Chlormalonsäurediethylester zudosieren.

Den Ansatz solange bei 105 °C nachröhren, bis keine Wärmeentwicklung mehr gemessen wird.

Die Reaktionszeit unter einem Eigendruck von knapp 6 bar betrug 12 Stunden.

Nach Reaktionsende wird der Ansatz auf RT abgekühlt und es werden 494,5 g Wasser zugeben, um die Suspension zu lösen. Die abgenommene Menge an Reaktionsgemisch für weitere DTA-Versuche protokollieren.

1618 g Reaktionsendgemisch mit 12 g (in 50 g Wasser löslichen) Kristallkomplexen wurde aufgearbeitet. Nach der Phasentrennung erhielt man 525 g organische und 1093 g wässrige Phase, wobei letztere kein Produkt enthielt.

Ausbeute: ca. 85% Produkt

m = 525 g GL₅₇₀ : 67,2 %

Exhibit B

Müh

PF-P+T VE

21 July 2000

Leverkusen B 202

Example for the fluorination of diethyl chloromalonate to give diethyl fluoromalonate

Into a pressure-resistant reaction vessel there are introduced 453 g of the adduct (3.21 mol) of 3.21 mol of triethylamine and 6.42 mol of hydrogen fluoride and a further 325 g of triethylamine (3.21 mol). The reaction vessel was sealed so as to be pressure-sealed and the contents were heated to 105°C. Within 6 hours, 541 g of diethyl chloromalonate (purity 77%; 2.14 mol) were metered in via a pump at 105°C, and the mixture was then stirred for a further 6 h at 105°C until the reaction was complete. After the reaction had ended, the mixture was cooled to 40°C, and 750 g of water were added in order to completely dissolve the suspension which was present after the reaction had ended. The organic bottom phase (440 g) was washed with 150 g of 15% strength sulphuric acid. This gave 420 g of a dark liquid which contains 73% of diethyl fluoromalonate (yield: approximately 81%), which was used in the next step partly directly and partly after distillation.

Müh

PF-P+T VE
21. Juli 2000
Leverkusen B 202

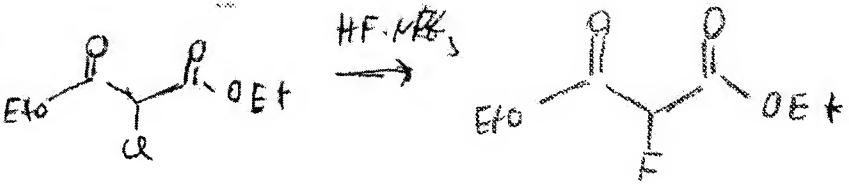
Beispiel für die Fluorierung von Chlormalonsäurediethylester zu Fluormalonsäurediethylester

In einem druckfesten Reaktionsbehälter werden 453 g des Additionsproduktes (3,21 Mol) von 3,21 Mol Triethylamin mit 6,42 Mol Fluorwasserstoff vorgelegt und mit weiteren 325 g Triethylamin (3,21 Mol) versetzt. Der Reaktionsbehälter wurde druckdicht verschlossen und der Behälterinhalt auf 105 °C aufgeheizt. Innerhalb von 6 h wurden 541 g Chlormalonsäurediethylester (Reinheit 77 %; 2,14 Mol) bei 105 °C über eine Pumpe zudosiert und anschließend weitere 6 h bei 105 °C bis zum vollständigen Umsatz gerührt. Nach Reaktionsende wurde auf 40 °C abgekühlt und 750 g Wasser zugegeben, um die nach Reaktionsende vorliegende Suspension vollständig aufzulösen. Die untere, organische Phase (440 g) wurde mit 150 g 15 % iger Schwefelsäure gewaschen. Man erhält 420 g einer dunklen Flüssigkeit, die 73 % Fluormalonsäurediethylester enthält (Ausbeute: ca. 81 %), der teilweise direkt, teilweise nach Destillation für die nächste Stufe verwendet wurde.

Exhibit C

Test as described by Müh

Operating instructions

 RD Laboratory Q 17 ZF-SFO 1 Leverkusen		Box/ Chamber:	Q17 No.:
Commissioned by: Dr. P. Plegl k.c.	J. No.:	Carried out by: H. Müller	
Decl/Acct: 2 F - SFF	Tel.:	Autoclave: 3811C	
Reaction conditions		(filled in by the RD Laboratory):	
Time:	Hours	Used at a rate of:	bar
Temp.:	see protocol	Run at:	bar
Pressure:	bar	Update (calc.):	bar
Starting materials:		MW	Test B as specified in WO 02/16304 (Müh)
Generally (cont.)	Designator (if appropriate manufacturer, partly other specifications)		
See protocol			
Risk statements (check where applicable, if appropriate add risk phrases)			
<input checked="" type="checkbox"/> poisonous	<input type="checkbox"/> explosive	<input type="checkbox"/> irritant	Other properties/statements:
<input type="checkbox"/> may cause cancer	<input type="checkbox"/> flammable	<input type="checkbox"/> substance not fully tested	
<input type="checkbox"/> mutagenic	<input type="checkbox"/> causes burns		
Safety phrases:			
Reaction equation/procedure:			
			
Test results (on enclosed copy, back to Q17):			
Conversion rate:	Other:		
Yield:			
Date: 30.10.00	Signature: 		
Copy for client			

Bayer

ZF-FGF

HD Laboratory Q 17

Leverkusen

No. 00-1434

Chamber / Box 24

Leverkusen, 06.11.2000

for Dr. Pleschke

Telephone

Test No.

Autoclave: 14864 ; litres: 3

Mat.: HC

bar: 300 ; Temp.: 300 °C

Time	Temperature		Heating	Pressure in bar			2	K
	external	internal		measured	injected	diff.		
Introduce triethylamine				flushed with N ₂				HF
10	40	62		0.7	58	to [illegible]	+	108
	42	61		1.4			+	108
	58	61		1.5			+	108
M	12	65		1.9			+	108
	22	59		1.4			+	108
	44	63		1.9			+	108
	58	62		2			+	108
12	12	59		1.9			+	108
	28	61		1.8			+	108
	43	61		1.7			+	108
	57	60		1.7			+	108
13	13	62		1.7			+	108
	Internal to			105 °C				
~ 80 mL/h	14	102		3.5				
	15	104.5		3.8				
								Start metering in (ester)

Pressure drop calc.: ?

found: 0027835 - 985

Bayer		HD-Labor Q17 ZF-SFO 1 Leverkusen		Betriebsanweisung			
		Box/ Kammer:	64	Q17-Nr.:		11/454	
Auftraggeber: Dr. Klegel, ka Abt./Kto.: 21-SFF		J.-Nr.:		Bearbeiter:			
		Tel.:		Autoklav:		APHC	
Reaktionsbedingungen:		(wurde im HD-Labor ausgeführt):			KL-Nr.:		
Zeit:	Std.	aufheizen mit:	bar	Bestückung:			
Temp.:	110 °C	fahren mit:	bar	Drehzahl:	UpM		
Druck:	bar	Aufnahme (ber.):	bar	GC-Probe(n):			
Einsatzstoffe:							
Menge (g/ml)	Bezeichnung (ggf. Hersteller, Reinheit, sonstige Spezifikationen)					MG	Mol
n,16 Vms. 11							
Gefahrenhinweise (zutreffendes ankreuzen, ggf. mit Sätzen ergänzen):							
<input type="checkbox"/> giftig	<input type="checkbox"/> explosionsgef.	<input type="checkbox"/> reizend	Sonstige Eigenschaften/Hinweise:				
<input type="checkbox"/> krebserr.	<input type="checkbox"/> entzündl.	<input type="checkbox"/> nicht vollständig geklärter Stoff					
<input type="checkbox"/> erbgutveränderl.	<input type="checkbox"/> giftig						
SI-Ratschläge (S-Sätze):							
Reaktionsgleichung/Durchführung:							
$ \begin{array}{c} \text{H}_2 \text{O} \\ \\ \text{C}_2\text{H}_5\text{OH} \\ \\ \text{C}_2\text{H}_5\text{OH} \\ \xrightarrow{\text{H}_2\text{SO}_4} \\ \text{C}_2\text{H}_5\text{OH} \\ \\ \text{C}_2\text{H}_5\text{OH} \\ \xrightarrow{\text{H}_2\text{SO}_4} \\ \text{C}_2\text{H}_5\text{OH} \\ \\ \text{C}_2\text{H}_5\text{OH} \end{array} $							
Versuchsergebnisse (auf beiliegender Kopie zurück an Q17):							
Umsatz:	Sonstiges:						
Ausbeute:							
Datum:	31.10.00						
	Unterschrift:						

Bayer		HD-Labor Q17 ZF-SFO 1 Leverkusen	Betriebsanweisung		
Auftraggeber: Dr. Plegl k.k.		Box/ Kammer: 64	Q17-Nr.: 01/1454		
Abl./Klo.: 2F-SFF		J.-Nr.: Tel.:	Bearbeiter: J. P. P. 10/1		
Reaktionsbedingungen:		(wird im HD-Labor ausgeführt).		KI.-Nr.:	
Zeit:	Std.	aufheizen mit:	bar	Bestückung:	
Temp.:	z. z. 100°C	fahren mit:	bar	Drehzahl:	
Druck:	bar	Aufnahme (bar):	bar	GC-Probe(n):	
Einsatzstoffe:					
Menge (g/ml)	Bezeichnung (ggf. Hersteller, Reinheit, sonstige Spezifikationen)			MG	
z. z. 100°C					
Gefahrenhinweise (zutreffendes ankreuzen, ggf. mit R-Sätzen ergänzen):					
Giftig	<input type="checkbox"/> explosionsgef.	<input type="checkbox"/> reizend	Sonstige Eigenschaften/Hinweise:		
<input type="checkbox"/> krebserg.	<input type="checkbox"/> entzündl.	<input type="checkbox"/> nicht vollständig gepr. Stoff			
<input type="checkbox"/> entzündbar	<input type="checkbox"/> ätzend				
Si-Ratschläge (S-Sätze):					
Reaktionsgleichung/Durchführung:					
Versuchsergebnisse (auf beiliegender Kopie zurück an Q17):					
Umsatz:	Sonstiges:				
Ausbeute:					
Datum:	Unterschrift:				

Autoklav: 144864 ; Ltr: 3
Mat: 4C
bar: 300 ; Temp: 300 °C

Zeit	Temperatur		Hzg.	Druck in bar			Dr	N ₂
	außen	innen		gem.	aufgedr.	Diff.		
Trichterklamme		ungeklemmt	N ₂ gegen					HF
10	40	62	0,7	5,9	bis Verl.	+	10g	
	43	61	1,4					
	52	61	1,5					
M	12	65	1,9					
	22	59	1,4					
	44	63	1,9					
	58	62	2					
11	72	59	1,9					
	88	61	1,8					
	45	61	1,7					
	57	60	1,7					
12	92	62	1,7					
	144	en	auf	105 °C				
280ml/h	14	102	3,5	8,9	Beg mit rütteln (ester)			
	15	104,5	3,8					

Druckabfall ber.:

gef.:

	außen	innen	gem.	aufgedr.	Diff.
16	20	106,7	4,06		
17	25	104,5	4,28		
18	20	104,8	4,61		
19	30	105,0	5,00		
20	25	105,0	5,6	Ende u. Pausa	
21	25	104,7	5,84		
22	25	104,7	6,06		
23	25	104,7	6,31		
0	25	104,7	6,64		
1	25	104,7	6,69		
2	25	104,7	6,90	Abkühlung auf 40%	
4	10	40,5	4,15	Beg. mit Pausa E-160	
	35	41,1	4,20		
5	10	38,9	4,53		
	20	37,1	4,75	Ende mit Pausa E-160	
Abkühlung auf RT					
Tafelklor mit 110g C-Wasser ausgespült					